

Answer 1:

Bibliographic Information

Effect of arsenic trioxide on HL-60 cells and HL-60 cell xenograft in nude mice. Li, Li; Meng, Fanyi; Fu, Yunbi; Sun, Qixin; Cai, Yanxia. Department of Hematology, Nanfang Hospital, Southern Medical University, Guangzhou, Peop. Rep. China. Shiyong Yixue Zazhi (2008), 24(11), 1883-1886. Publisher: Shiyong Yixue Zazhi Bianjibu, CODEN: SYZAFM ISSN: 1006-5725. Journal written in Chinese. AN 2008:976166 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The objective was to assess the effect of arsenic trioxide on proliferation and apoptosis of HL-60 cells, and to investigate its antitumor efficacy and adverse effects for HL-60-bearing nude mice. HL-60 cells were treated with arsenic trioxide for 48 h and the cell proliferation was analyzed with MTT assay, and the cell apoptosis was detected by Hoechst 33342 staining, DNA gel electrophoresis, fluorescence microscopy and flow cytometry. Nude mice bearing HL-60 cell xenografts were randomized into 2 groups to receive treatment with normal saline and arsenic trioxide. The tumor growth inhibition and general condition of the nude mice were observed. Arsenic trioxide could effectively inhibit HL-60 cell proliferation and induce cell apoptosis. At the concentrations of 5 $\mu\text{mol/L}$ to 50 $\mu\text{mol/L}$, it had conspicuous dose-dependent effect. It also could inhibit the growth of the transplanted tumors and prolong the survival of nude mice. The administration was well tolerated by the mice. Arsenic trioxide could significantly inhibit HL-60 cell proliferation and induce cell apoptosis both in vitro and in vivo, and there were no significant adverse effects.

Answer 2:

Bibliographic Information

Effect of arsenic trioxide on vascular endothelial cell proliferation and expression of vascular endothelial growth factor receptors Flt-1 and KDR in gastric cancer in nude mice. Xiao, Yan-Feng; Wu, De-Dong; Liu, Shan-Xi; Chen, Xi; Ren, Li-Fen. Department of Pediatrics, The Second Affiliated Hospital of Medical College, Xi'an Jiaotong University, Xi'an, Shaanxi Province, Peop. Rep. China. World Journal of Gastroenterology (2007), 13(48), 6498-6505. Publisher: World Journal of Gastroenterology, CODEN: WJGAF2 ISSN: 1007-9327. Journal written in English. CAN 148:346136 AN 2008:170726 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Aim: To investigate the effect of arsenic trioxide (As_2O_3) on expression of vascular endothelial growth factor receptor-1 (VEGFR-1, Flt-1) and VEGFR-2 (KDR) in human gastric tumor cells and proliferation of vascular endothelial cells. **Methods:** The solid tumor model was formed in nude mice with the gastric cancer cell line SGC-7901. The animals were treated with As_2O_3 . Microvessel density (MVD) and expression of Flt-1 and KDR were detected by immunofluorescence laser confocal microscopy. SGC-7901 cells were treated respectively by exogenous recombinant human VEGF165 or VEGF165 + As_2O_3 . Cell viability was measured by MTT assay. Cell viability of ECV304 cells was measured by MTT assay, and cell cycle and apoptosis were analyzed using flow cytometry. **Results:** The tumor growth inhibition was 30.33% and 50.85%, respectively, in mice treated with As_2O_3 2.5 and 5 mg/kg. MVD was significantly lower in arsenic-treated mice than in the control group. The fluorescence intensity levels of Flt-1 and KDR were significantly less in the arsenic-treated mice than in the control group. VEGF165 may accelerate growth of SGC7901 cells, but As_2O_3 may disturb the stimulating effect of VEGF165. ECV304 cell growth was suppressed by 76.51%, 71.09% and 61.49% after 48 h treatment with As_2O_3 at 0.5, 2.5 and 5 $\mu\text{mol/L}$, respectively. Early apoptosis in the As_2O_3 -treated mice was 2.88-5.1 times higher than that in the controls, and late apoptosis was 1.17-1.67 times higher than that in the controls. **Conclusion:** Our results showed that As_2O_3 delays tumor growth, inhibits MVD, down-regulates Flt-1 and KDR expression, and disturbs the stimulating effect of VEGF165 on the growth of SGC7901 cells. These results suggest that As_2O_3 might delay growth of gastric tumors through inhibiting the paracrine and autocrine pathways of VEGF/VEGFRs.

Answer 3:

Bibliographic Information

Effect of bortezomib used alone or in combination with arsenic trioxide on HL-60 cell xenograft in nude mice. Li, Li; Meng, Fan-yi; Fu, Yun-bi; Cai, Yan-xia; Sun, Qi-xin. Department of Hematology, Nanfang Hospital, Southern Medical University, Guangzhou, Peop. Rep. China. Nanfang Yike Daxue Xuebao (2007), 27(10), 1504-1506. Publisher: Nanfang Yike Daxue Xuebao Bianjibu, CODEN: NYDXAN ISSN: 1673-4254. Journal written in Chinese. CAN 148:345912 AN 2007:1359310 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The study assessed the antitumor efficacy and adverse effects of bortezomib either used alone or in combination with arsenic trioxide for transplanted tumor in nude mice. Nude mice bearing HL-60 cell xenografts were randomized into 4 groups to receive treatment with normal saline, bortezomib, arsenic trioxide, bortezomib plus arsenic trioxide. The tumor growth inhibition and general condition of the nude mice were obsd., and in situ TUNEL assay and immunohistochem. were performed on the transplanted tumors. Bortezomib alone and in combination with arsenic trioxide could both inhibit the growth of the transplanted tumors, prolong the survival of the nude mice, and induce cell apoptosis and growth inhibition of the HL-60 cells in vivo, and the combined administration exhibited even better effects. The administration was well tolerated with causing manifest vital organ damages in the mice. Bortezomib in combination with arsenic trioxide has significant antitumor effect in nude mice bearing HL-60 cell xenografts possibly by inducing HL-60 cell apoptosis and growth inhibition without produceing no significant adverse effects.

Answer 4:

Bibliographic Information

Antimyeloma effects of arsenic trioxide are enhanced by melphalan, bortezomib and ascorbic acid. Campbell, Richard A.; Sanchez, Eric; Steinberg, Jeffrey A.; Baritaki, Stavroula; Gordon, Melinda; Wang, Cathy; Shalitin, Dror; Chen, Haiming; Pang, Shen; Bonavida, Benjamin; Said, Jonathan; Berenson, James R. Institute for Myeloma & Bone Cancer Research, West Hollywood, The University of California, Los Angeles, CA, USA. British Journal of Haematology (2007), 138(4), 467-478. Publisher: Blackwell Publishing Ltd., CODEN: BJHEAL ISSN: 0007-1048. Journal written in English. CAN 147:479931 AN 2007:1032111 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Arsenic trioxide (ATO) induces apoptosis of malignant plasma cells through multiple mechanisms, including inhibition of DNA binding by nuclear factor kappa-B, a key player in the development of chemoresistance in multiple myeloma (MM). This activity suggests that ATO may be synergistic when combined with other active antimyeloma drugs. To evaluate this, we examd. the antimyeloma effects of ATO alone and in combination with bortezomib, melphalan and ascorbic acid (AA) both in vitro and in vivo using a severe combined immunodeficient (SCID)-hu murine myeloma model. Marked synergistic antimyeloma effects were demonstrated when human MM Los Angeles xenograft IgG lambda light chain (LAG λ -1) cells were treated in vitro with ATO and any one of these agents. SCID mice bearing human MM LAG λ -1 tumors were treated with single-agent ATO, bortezomib, melphalan, or AA, or combinations of ATO with either bortezomib or melphalan and AA. Animals treated with any of these drugs alone showed tumor growth and increases in paraprotein levels similar to control mice, whereas animals treated with ATO-contg. combinations showed markedly suppressed tumor growth and significantly reduced serum paraprotein levels. These in vitro and in vivo results suggest that addn. of ATO to other antimyeloma agents may result in improved outcomes for patients with relapsed or refractory MM.

Answer 5:

Bibliographic Information

Synergistic therapeutic effect of arsenic trioxide and radiotherapy in BALB/C nude mice bearing nasopharyngeal carcinoma xenografts. Xie, L. X.; Lin, X. H.; Li, D. R.; Chen, J. Y.; Hong, C. Q.; Du, C. W. Laboratory of Cancer Research, Tumor Hospital, Shantou University Medical College, Shantou, Peop. Rep. China. Experimental Oncology (2007), 29(1), 45-48.

Publisher: Morion LLC, CODEN: EOXNAQ ISSN: 1812-9269. Journal written in English. CAN 147:157755 AN 2007:571290
CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

It has been shown that arsenic trioxide (ATO) induced apoptosis in human nasopharyngeal carcinoma cells and inhibited the growth of nasopharyngeal carcinoma xenografts (NPCX) in nude mice. Aim: The present study was designed to det. whether ATO at the non-toxic dose level could potentiate the therapeutic effectiveness of radiation therapy in nasopharyngeal carcinoma, using a BALB/C nude mouse xenograft model. Methods: The mice bearing NPCX were treated with radiation alone (2, 4, and 6 Gy), ATO alone (4 mg/kg/day \times 6 days), and ATO plus radiation at the same dosage levels. Time of tumor growth delay (defined as the time necessary for the tumor to grow four-fold of its initial vol. after, compared with untreated tumors) and toxic effects were detd. Results: The low dose ATO alone has no pronounced effects on tumor growth delay compared to untreated control. However, compared with radiation alone, the combined regimen delayed the tumor growth by 2-10 days and had no significant toxic effects such as the liver function damage. Conclusions: Combination of ATO at non-toxic dose level and radiation has synergistic effects on tumor growth inhibition in vivo and is well tolerated.

Answer 6:

Bibliographic Information

Inhibitory effects and mechanism of arsenic trioxide on the growth of melanoma B16 cells. Xia, Jun; Chen, Junxia; Yu, Lihua; Cui, Xiuyun; Chen, Zhiwen. Department of Biochemistry and Molecular Biology, Bengbu Medical College, bengbu, Peop. Rep. China. Zhongguo Yaolixue Tongbao (2004), 20(9), 1054-1058. Publisher: Anhui Yike Daxue Linchuan Yaoli Yanjiuso, CODEN: ZYTOE8 ISSN: 1001-1978. Journal written in Chinese. CAN 144:246707 AN 2005:1346452 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The growth inhibition and anti-angiogenesis of arsenic trioxide(As₂O₃) on B 16 cells xenografts in C57BL/6J mice and the effects of As₂O₃ on cell proliferation, cell morphol., cell cycle and apoptosis were studied in vitro. Mice melanoma cell line B16 was transplanted into C57BL/6J mice. The wt. of tumor and percent of tumor development were examd. after As₂O₃ i.p. administration. HE staining and immunohistochem. for VIII-R Ag were performed to detect the microvessel d. in tumor tissues. CellTiter 96 Aq. One was used to det. the cell proliferation. Giemsa and Feulgen staining were used to observe the morphol. changes of the cells. Cell cycle and apoptosis were analyzed by flow cytometry(FCM). As₂O₃ significantly inhibited the tumor growth in vivo, with an inhibitory rate of 81.61%. The microvessel d. in tumor tissues was obviously reduced after treated with As₂O₃. There was obviously a concn.-dependent relationship between As₂O₃ and the inhibition of B16 cells proliferation (P < 0.01). IC₅₀ was 32.99 μ mol/L. Cell morphol. results showed that cell d. was decreased, contents of DNA were lowed, nuclear area was became smaller, and cells had higher differentiation than that of the control group. FCM demonstrated that As₂O₃ at 20 μ mol/L arrest B16 cells in G₀-G₁ phase, but higher dose As₂O₃ at 40 μ mol/L might induce apoptosis of B16 cells. The results suggest that As₂O₃ can inhibit B16 melanoma growth by means of anti-angiogenesis, cell proliferation inhibition, cell cycle block, and apoptosis.

Answer 7:

Bibliographic Information

Effects of arsenic trioxide on hTERT expression and telomerase activity of human colonic carcinoma xenograft in nude mice. Wang, Nan-yao; Liu, Lin; Qiu, Shao-min; Zhao, Wei; Qin, Shu-kui; Chen, Hui-ying; Li, Su-yi. Department of Oncology, Zhongda Hospital, Southeast University, Nanjing, Peop. Rep. China. Dongnan Daxue Xuebao, Yixueban (2005), 24(3), 168-170. Publisher: Dongnan Daxue Xuebao, Yixueban Bianjibu, CODEN: DDXYA5 ISSN: 1671-6264. Journal written in Chinese. CAN 143:359551 AN 2005:573157 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The influence of As₂O₃ on human telomerase reverse transcriptases (hTERT) expression and telomerase activity of human colonic carcinoma xenograft in nude mice was studied. As₂O₃ was i.v. injected into nude mice in the established human colonic carcinoma xenograft model. Telomerase activity was detected by silver stain with TRAP. The expression of hTERT was detected by reverse transcription polymerase chain reaction (RT-PCR). The telomerase activity and hTERT expression of NS control group and 5-FU group were highly expressed while those of low and high As₂O₃ concn. groups were both obviously inhibited. As₂O₃ can greatly inhibit telomerase activity and hTERT expression of human colonic carcinoma xenograft in nude mice.

Answer 8:

Bibliographic Information

Arsenic trioxide induces differentiation of human nasopharyngeal carcinoma in BALB/C nude mice xenograft model. Du, Caiwen; Li, Derui; Lin, Yingcheng; Wu, Mingyao. Medical College, Shantou University, Shantou, Guangdong Province, Peop. Rep. China. Aizheng (2003), 22(1), 21-25. Publisher: Sun Yat-sen Daxue, Aizheng Zhongxin, CODEN: AIZHE4 ISSN: 1000-467X. Journal written in Chinese. CAN 142:211575 AN 2004:938063 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

There is evidence that arsenic trioxide (As₂O₃) induces differentiation of leukemia cells; however, little is known about its effect on solid tumors. The aim of this study was to investigate whether As₂O₃ can induce cell differentiation and its assocn. with growth inhibition in human nasopharyngeal carcinoma using BALB/C nude mice xenograft model. Poorly differentiated human nasopharyngeal squamous carcinoma cells from CSNE-1 cell strain were transplanted s.c. to BALB/C nude mice to produce tumors. As₂O₃ at a dose of 5 mg · (kg·d)⁻¹ was given i.p. for 10 consecutive days, and then 3 times a week for the following 3 wk. The xenograft tumor growth in mice was obsd. after drug administration. The morphol. changes of the tumors were examd. under light and electron microscopy. Proliferating cell nuclear antigen (PCNA) expression was detd. by immunohistochem. As₂O₃ at dose of 5mg · (kg·d)⁻¹ significantly inhibited the tumor growth in vivo, with a inhibitory rate of 75.4%. Remarkable cell differentiation induced by As₂O₃ was obsd. under light microscope and transmission electron microscope, which was characterized by keratinization of tumor cells, decreased nuclear/cytoplasm ratio, increased cytoplasmic organelles and rich tonofibrils in cytoplasm. Desmosomes and micro-processes were much more frequently obsd. in tumors treated with As₂O₃. Significantly decreased PCNA expression was obsd. in As₂O₃-treated tumor cells. The PCNA-pos. cell index (PI) was (53.6±7.0)% in As₂O₃-treated mice, and (95.2±5.0)% in control, resp. The growth of human nasopharyngeal carcinoma xenograft in BALB/C nude mice can be significantly inhibited by As₂O₃, which might be related to the cell differentiation induced by As₂O₃.

Answer 9:

Bibliographic Information

Increased cure rate of glioblastoma using concurrent therapy with radiotherapy and arsenic trioxide. Ning, Shoucheng; Knox, Susan J. Department of Radiation Oncology, Stanford University Medical Center, Stanford, CA, USA. International Journal of Radiation Oncology, Biology, Physics (2004), 60(1), 197-203. Publisher: Elsevier Inc., CODEN: IOBPD3 ISSN: 0360-3016. Journal written in English. CAN 142:406686 AN 2004:710637 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Purpose. Patients with glioblastoma multiforme (GBM) do extremely poorly despite aggressive therapy with surgery, radiotherapy (RT), and chemotherapy. In an effort to increase the efficacy of therapy for GBM, we studied the efficacy of arsenic trioxide (ATO) combined with high-dose RT in GBM cells in vitro and GBM xenograft tumors in nude mice. **Methods and materials.** Human glioblastoma cell line SNB75 cells were irradiated in vitro with doses of 0-15 Gy with or without ATO. Clonogenic assays were used to generate radiation survival curves. Intracellular reactive oxygen species and apoptosis induced by ATO and RT were measured. The therapeutic efficacy of ATO alone, local tumor RT alone, and the combined therapy was tested in nude mice bearing established s.c. SNB75 tumors. A single RT dose of 20 Gy was administered locally to tumors. ATO at 10 mg/kg was injected i.p. 10 min after RT for the in vivo expts. **Results.** Radiation survival curves of GBM SNB75 cells demonstrated that a dose of 0.2 µM ATO increased

radiation-induced cell killing by 2 logs at 10 Gy. ATO at 1 μ M decreased survival from 4×10^{-2} after 7 Gy of RT alone to 4×10^{-5} . A time-course expt. demonstrated that the greatest level of cell killing occurred when ATO was administered immediately before or within 2 h after RT. To test the therapeutic efficacy of this combined treatment regimen in vivo, nude mice with established SNB75 GBM tumors were treated with a single local tumor dose of 20 Gy of RT with or without ATO (10 mg/kg \times two doses) administered weekly. Appropriate control groups were included as well. ATO alone did not inhibit tumor growth. RT at 20 Gy alone inhibited tumor growth by 45 days, with regrowth of tumors thereafter. The combination of RT and ATO resulted in complete regression of the tumors in 4 of 5 mice without tumor regrowth for up to 4 mo. The fifth mouse in the combined treatment group had a 90% redn. in tumor size without progression during the 4-mo follow-up period.

Furthermore, ATO alone and in combination with RT did not produce any obvious signs of toxicity. Conclusion. These results have demonstrated that ATO increases intracellular levels of reactive oxygen species, induces apoptosis, and enhances the radiation cell killing of GBM cells. RT combined with ATO was an effective treatment for GBM tumors in this preclin. model. These preclin. results are encouraging and provide a rationale for further study of ATO combined with RT for the treatment of GBM and other histol. types of brain cancer using a variety of RT schemes.

Answer 10:

Bibliographic Information

Inhibition of NF- κ B essentially contributes to arsenic-induced apoptosis. Mathas, Stephan; Lietz, Andreas; Janz, Martin; Hinz, Michael; Jundt, Franziska; Scheidereit, Claus; Bommert, Kurt; Doerken, Bernd. Max-Delbrueck-Center for Molecular Medicine, Berlin, Germany. Blood (2003), 102(3), 1028-1034. Publisher: American Society of Hematology, CODEN: BLOOAW ISSN: 0006-4971. Journal written in English. CAN 140:22753 AN 2003:594553 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Arsenic can induce apoptosis and is an efficient drug for the treatment of acute promyelocytic leukemia. Currently, clin. studies are investigating arsenic as a therapeutic agent for a variety of malignancies. In this study, Hodgkin/Reed-Sternberg (HRS) cell lines served as model systems to characterize the role of nuclear factor- κ B (NF- κ B) in arsenic-induced apoptosis. Arsenic rapidly down-regulated constitutive I κ B kinase (IKK) as well as NF- κ B activity and induced apoptosis in HRS cell lines contg. functional I κ B proteins. In these cell lines, apoptosis was blocked by inhibition of caspase-8 and caspase-3-like activity. Furthermore, arsenic treatment down-regulated NF- κ B target genes, including tumor necrosis factor- α receptor-assocd. factor 1 (TRAF1), c-IAP2, interleukin-13 (IL-13), and CCR7. In contrast, cell lines with mutated, functionally inactive I κ B proteins or with a weak constitutive IKK/NF- κ B activity showed no alteration of the NF- κ B activity and were resistant to arsenic-induced apoptosis. A direct role of the NF- κ B pathway in arsenic-induced apoptosis is shown by transient overexpression of NF- κ B-p65 in L540Cy HRS cells, which protected the cells from arsenic-induced apoptosis. In addn., treatment of NOD/SCID mice with arsenic trioxide induced a dramatic redn. of xenotransplanted L540Cy Hodgkin tumors concomitant with NF- κ B inhibition. We conclude that inhibition of NF- κ B contributes to arsenic-induced apoptosis. Furthermore, pharmacol. inhibition of the IKK/NF- κ B activity might be a powerful treatment option for Hodgkin lymphoma.

Answer 11:

Bibliographic Information

Inhibition of growth of human nasopharyngeal cancer xenografts in SCID mice by arsenic trioxide. Li, Derui; Du, Caiwen; Lin, Yingchen; Wu, Mingyao. Department of Radiation Oncology, Cancer Hospital of Shantou University Medical College, Shantou, Peop. Rep. China. Tumori (2002), 88(6), 522-526. Publisher: Il Pensiero Scientifico Editore, CODEN: TUMOAB ISSN: 0300-8916. Journal written in English. CAN 139:254869 AN 2003:171412 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

It is known that arsenic trioxide (As₂O₃) can induce clin. remission in patients suffering from acute promyelocytic leukemia. It has been suggested that the agent might also be effective against other malignancies. This study was done to explore the efficacy of

As₂O₃ in the treatment of human nasopharyngeal cancer xenografts in SCID (severe combined immunodeficiency) mice. Human nasopharyngeal cancer cells from the CSNE-1 cell line were implanted s.c. into SCID mice to produce tumors. The tumor inhibitory rate in vivo was assessed after i.p. administration of As₂O₃. Histopathol. changes in the tumor tissues and the toxicity of As₂O₃ to the liver, heart and kidneys of the host mice were also investigated. At doses of 1 mg/kg and 5 mg/kg As₂O₃ induced apoptosis in nasopharyngeal carcinoma cells. At 5 mg/kg As₂O₃ also induced cancer cell differentiation, it reduced the PCNA expression, and inhibited tumor growth. The tumor growth inhibitory rate in this exptl. group was 76.02%. No nephrotoxicity was obsd. histol. at these dose levels but some pathol. changes in liver and cardiac tissues were found. As₂O₃ proved lethal to the SCID mice at a dose of 10 mg/kg. Conclusion: As₂O₃ has an inhibitory effect on human nasopharyngeal carcinoma xenografts in SCID mice. The mechanism of antitumor activity may be due, at least in part, to the induction of apoptosis and differentiation in cancer cells.

Answer 12:

Bibliographic Information

The inhibition of growth and angiogenesis in heterotransplanted esophageal carcinoma via intratumoral injection of arsenic trioxide. Shen Zhong-Ying; Shen Jian; Chen Ming-Hua; Wu Xian-Ying; Wu Min-Hua; Zeng Yi
Department of Pathology, College of Medicine, Shantou University, Shantou 515031, PR China.
zhongyingshen@yahoo.com Oncology reports (2003), 10(6), 1869-74. Journal code: 9422756. ISSN:1021-335X.
Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID
14534710 AN 2003472586 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

To investigate the antitumor action of arsenic trioxide (As₂O₃) by intratumoral injection into solid tumors, tumor growth inhibition (TGI) and angiogenesis of heterotransplanted esophageal carcinoma in mice was carried out. The cultured human esophageal carcinoma cells were inoculated into both laterals of the abdominal wall of severe combined immunodeficient (SCID) mice. When both lateral tumors had grown to about 10x8x5 mm(3), the right tumors were treated with an intratumoral injection of As₂O₃ in dosage of 1, 5 and 10 microg per day, respectively, for 10 days sequentially. Left tumors were treated with PBS (phosphate buffer solution) as control. The weight of transplanted tumor masses were measured and counted for TGI. The tissue of tumor, liver, kidney, heart, lung and brain was examined histopathologically and tumor tissues were examined by light- or electron-microscope. Ki-67 and CD34 were assessed by immunohistochemistry and positive nuclei of Ki-67 and microvessel density (MVD) labeled by CD34 were measured. The results revealed that on the 20th day after the first injection, As₂O₃-treated tumors were suppressed markedly as compared with the contrarily situated tumor, accompanied by a marked apoptosis and necrosis in tumor cells. The tissue of liver, kidney, heart, lung and brain was unaffected by As₂O₃. MVD in tumor tissue was decreased in the right side tumor with the significant difference in the 5 micro g and 10 micro g group (p<0.01). TGI was 5.80 (p>0.05), 58.66 (p<0.01) and 73.97% (p<0.01) in the 1, 5 and 10 micro g groups respectively, but 2.21% (p>0.05) in the control group. Conclusively, a repeated administration of As₂O₃ (5 and 10 microg x 10) induced an increase of tumor growth inhibition and decrease of angiogenesis in the solid tumor in tumor progressive periods. These results suggest that intra-tumoral injection of As₂O₃ may be investigated as a modality to treat some solid tumors.